

## REMARKS

### Amendments to Claims

Several claims have been amended to set forth proper Markush group language and to correct other minor informalities not affecting their scope.

### Requirement for Restriction

Restriction was required under 35 U.S.C. § 121 and 372 to one of the following groups of inventions:

- Group I: Claims 1, 4-12 and 15-23 in part, drawn to an isolated polynucleotide which codes for at least a part of a bifunctional hybrid active-site serine  $\beta$ -lactamase protein, wherein  $\beta$ -lactamase protein is bearing at least one heterologous sequence.
- Group II: Claim 25, drawn to an isolated polypeptide comprising at least a part of a bifunctional hybrid active-site serine  $\beta$ -lactamase protein, wherein  $\beta$ -lactamase protein is bearing at least one heterologous sequence.

### Response to Restriction Requirement

In response to the restriction requirement, Applicants elect Group I, encompassing Claims 1, 4-12 and 15-23. This election is made with traverse for the reasons discussed hereinbelow.

### Election of Sequence and Species Requirements

#### Sequence

Applicants were required to elect a combination of two sequences encoding for one  $\beta$ -lactamase protein and one heterologous sequence.

Applicants elect the  $\beta$ -lactamase protein encoded by SEQ ID NO:2 and the heterologous nucleotide sequence of SEQ ID NO:25.

#### Species

Applicants were required to elect a single species of heterologous sequence from among species (a) through (j) listed on page 6 of the communication from the Office. Applicants elect species (i), "being a specific partner for any polypeptide or any ligand." Claims 1, 4-12, 15-23 and 25 read on the elected species.

### Traversal of Restriction Requirement

Notwithstanding the foregoing elections, Applicants traverse the requirement insofar as it requires restriction between Groups I and II because the inventions in these groups do relate to a single general inventive concept as envisaged by PCT Rule 13.1 and Rule 13.2.

The Office Action states that the inventions listed as Group I-II do not relate to a single general concept under PCT Rule 13.1 because, under PCT Rule 13.2, the polynucleotides of Group I and the polypeptides of Group II do not share a corresponding technical feature. The Examiner reached this conclusion based on an allegation that the shared technical feature of polynucleotides encoding at least a part of a bifunctional hybrid active-site serine  $\beta$ -lactamase protein, wherein the  $\beta$ -lactamase protein is bearing at least one heterologous sequence, is anticipated by WO 03/105753. However, as explained below, both groups of claims share a corresponding technical feature that is neither anticipated nor rendered obvious by this reference.

Both groups of claims recite that the  $\beta$ -lactamase protein bears the heterologous sequence in a region located between two neighboring alpha helices of the  $\beta$ -lactamase sequence. Both groups of claims further recite that the region is forming a juncture between the alpha helices of active-site serine  $\beta$ -lactamases, wherein said alpha helices correspond to the last two alpha helices before the alpha/beta domain. As set forth in paragraphs [0039] and [0040] of the specification as filed, the Applicants have succeeded in identifying and creating, in a loop diametrically opposed to the active enzyme site, a region that is particularly favorable for internalizing large exogenous sequences of peptides. Large polypeptides internalized in the context of the last two alpha helices before the alpha/beta domain, as recited in both groups of claims, are able to adopt a folding close to their native conformation, whereby their biological activity is retained. Thus, the claims in Groups I and II share the technical feature of the  $\beta$ -lactamase protein bearing the heterologous sequence in a region located between two neighboring alpha helices of the  $\beta$ -lactamase sequence, wherein said alpha helices correspond to the last two alpha helices before the alpha/beta domain. As this technical feature is shared by both groups of claims and is neither anticipated nor rendered obvious by WO 03/105753, the Applicants respectfully request that the restriction requirement be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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